CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 040106

Trade Name : OXYCODONE AND ACETAMINOPHEN CAPSULES USP 5MG/500MG

Generic Name: Oxycodone and Acetaminophen Capsules USP 5mg/500mg

Sponsor : Vintage Pharmaceuticals, Inc.

Approval Date: July 30, 1996

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 040106

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				
Approvable Letter				
Final Printed Labeling	X			
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)				
Bioequivalence Review(s)	X			
Administrative Document(s)				
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 040106

APPROVAL LETTER

ANDA 40-106

JUL 30 1996

Vintage Pharmaceuticals, Inc.
Attention: Rebecca A. Thurman
3241 Woodpark Boulevard
Charlotte, NC 28206

Dear Madam:

This is in reference to your abbreviated new drug application dated June 9, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Oxycodone and Acetaminophen Capsules USP, 5 mg (as Oxycodone Hydrochloride)/ 500 mg.

Reference is also made to your amendments dated September 11, 1995, October 2, 1995, December 11, 1995, June 10, 1996, June 20, 1996, July 8, 1996 and July 16, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Oxycodone and Acetaminophen Capsules USP, 5 mg (as Oxycodone Hydrochloride)/500 mg, to be bioequivalent and, therefore, therapeutically equivalent to those of the listed drug (Tylox Capsules, of R.W. Johnson Pharmaceutical Research Institute, Division of Ortho Pharmaceutical Corp.). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253

(Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/ 7/30/96

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040106

FINAL PRINTED LABELING

OXYCODONE* AND ACETAMINOPHEN CAPSULES, USP

C II

JUL 30 1996

DESCRIPTION

Each capsule, for oral administration, contains:

Oxycodone Hydrochloride, USP (equivalent to 4.4815 mg Oxycodone)	5 mg
Acetaminophen, USP	500 mg

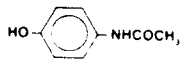
*WARNING- May be habit forming

In addition each capsule contains the following inactive ingredients: croscarmellose sodium, magnesium stearate and microcrystalline cellulose.

Capsule ingredients: black ink, FD & C Red #40, gelatin, silicon dioxide, sodium lauryl sulfate and titanium dioxide.

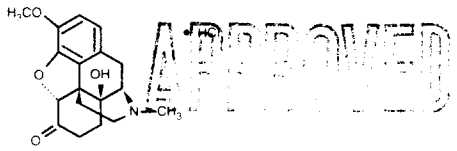
Black ink ingredients: D & C Yellow #10 Lake, FD & C Blue #1 Lake, FD & C Blue #2 Lake, FD & C Red #40 Lake, n-butyl alcohol, pharmaceutical glaze, propylene glycol and synthetic black iron oxide.

The acetaminophen component is 4'- hydroxyacetanilide, a white odorless, crytalline powder, possessing a slightly bitter taste, and having the following structural formula:



$C_8H_9NO_2$ MW = 151.17

The oxycodone component is 14-hydroxydihydrocodeinone, a white, odorless, crystalline powder having a saline bitter taste. It is derived from the opium alkaloid thebaine, and may be represented by the following structural formula:



$C_{18}H_{21}NO_4$ MW = 315.83

CLINICAL PHARMACOLOGY

The principal ingredient, oxycodone, is a semisynthetic narcotic analgesic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value of the oxycodone in this product are analgesia and sedation.

Oxycodone is similar to codeine and methadone in that it retains at least one-half of its analgesic activity when administered orally.

Acetaminophen is a non-opiate, non-salicylate analgesic and antipyretic.

INDICATIONS AND USAGE

Oxycodone and Acetaminophen Capsules are indicated for the relief of moderate to moderately severe pain.

CONTRAINDICATIONS

Oxycodone and Acetaminophen Capsules should not be administered to patients who are hypersensitive to any component.

WARNINGS

Drug Dependence

Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of this drug and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, Oxycodone and Acetaminophen Capsules are subject to the Federal Controlled Substance Act (Schedule II).

PRECAUTIONS

General

Head Injury and Increased Intracranial Pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions: The administration of products containing oxycodone or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special Risk Patients: Oxycodone and Acetaminophen Capsules should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethal stricture.

Information for Patients

Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using Oxycodone and Acetaminophen Capsules should be cautioned accordingly.

Drug Interactions

Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with Oxycodone and Acetaminophen Capsules may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

The concurrent use of anticholinergics with narcotics may produce paralytic ileus.

Pregnancy

Teratogenic Effects: Pregnancy Category C: Animal reproductive studies have not been conducted with Oxycodone and Acetaminophen Capsules. It is also not known whether Oxycodone and Acetaminophen Capsules can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Oxycodone and Acetaminophen Capsules should not be given to a pregnant woman unless in the judgment of the physician, the potential benefits outweigh the possible hazards.

Nonteratogenic Effects: Use of narcotics during pregnancy may produce physical dependence in the neonate.

Labor and Delivery

As with all narcotics, administration of Oxycodone and Acetaminophen Capsules to the mother shortly before delivery may result in some degree of respiratory depression in the newborn and the mother, especially if higher doses are used.

Nursing Mothers

It is not known whether the components of this product are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Oxycodone and Acetaminophen Capsules are administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus. At higher doses, oxycodone has most of the disadvantages of morphine including respiratory depression.

DRUG ABUSE AND DEPENDENCE

Oxycodone and Acetaminophen Capsules are a Schedule II controlled substance.

Oxycodone can produce drug dependence and has the potential for being abused. (See WARNINGS)

OVERDOSAGE

Acetaminophen

Signs and Symptoms: In acute acetaminophen overdosage, dose-dependent potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma and thrombocytopenia may also occur.

In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10 grams and fatalities with less than 15 grams. Importantly, young children seem to be more resistant than adults to the hepatotoxic effect of an acetaminophen overdose.

Despite this, the measures outlined below should be initiated in any adult or child suspected of having ingested an acetaminophen overdose.

Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Treatment: The stomach should be emptied promptly by lavage or by induction of emesis with syrup of ipecac. Patients' estimates of the quantity of a drug ingested are notoriously unreliable. Therefore, if an acetaminophen overdose is suspected, a serum acetaminophen assay should be obtained as early as possible, but no sooner than four hours following ingestion. Liver function studies should be obtained initially and repeated at 24-hour intervals.

The antidote, N-acetylcysteine, should be administered as early as possible, and within 16 hours of the overdose ingestion for optimal results. Following recovery, there are no residual, structural, or functional hepatic abnormalities.

Oxycodone

Signs and Symptoms: Serious overdosage with oxycodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment: Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of naloxone hydrochloride (usual initial adult dose 0.4 mg to 2 mg) should be administered preferably by the intravenous route, and simultaneously with efforts at respiratory resuscitation (see package insert). Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric emptying may be useful in removing unabsorbed drug.

DOSAGE AND ADMINISTRATION

Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics.

Oxycodone and Acetaminophen Capsules are given orally. The usual adult dosage is one Oxycodone and Acetaminophen Capsule every 6 hours as needed for pain.

HOW SUPPLIED

Oxycodone Hydrochloride and Acetaminophen Capsules, USP, 5 mg/500 mg, supplied as a red capsule, imprinted 4832/V in bottles of 100, 500 and 1000. Dispense in tight, light-resistant container as defined in the official USP.

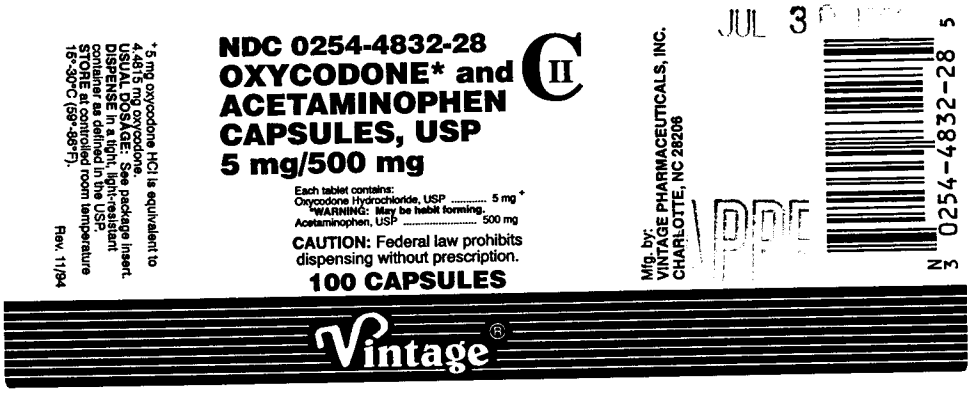
Store at controlled room temperature 15°–30° C, (59°–86° F), as defined in the USP. Protect from moisture.

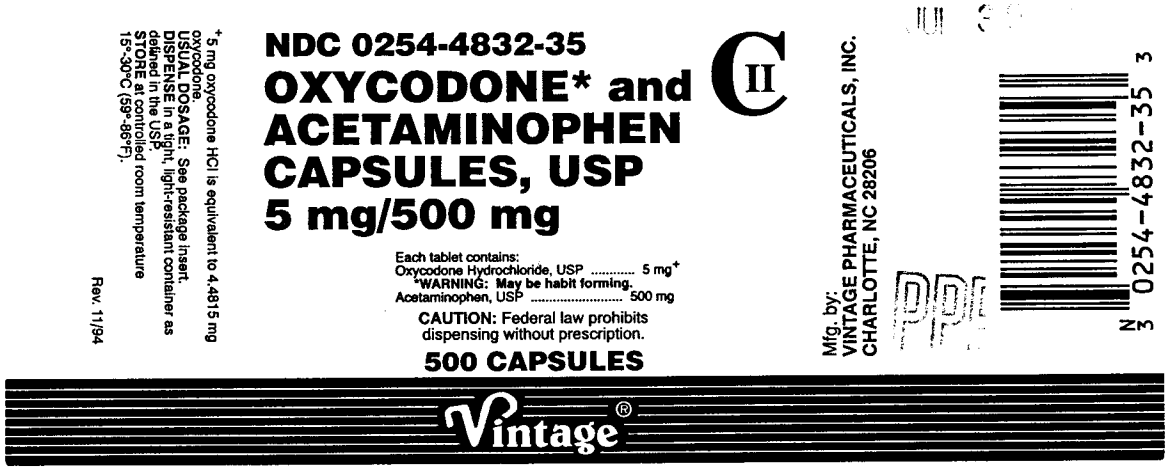
Vintage Pharmaceuticals, Inc.
Charlotte, NC 28206

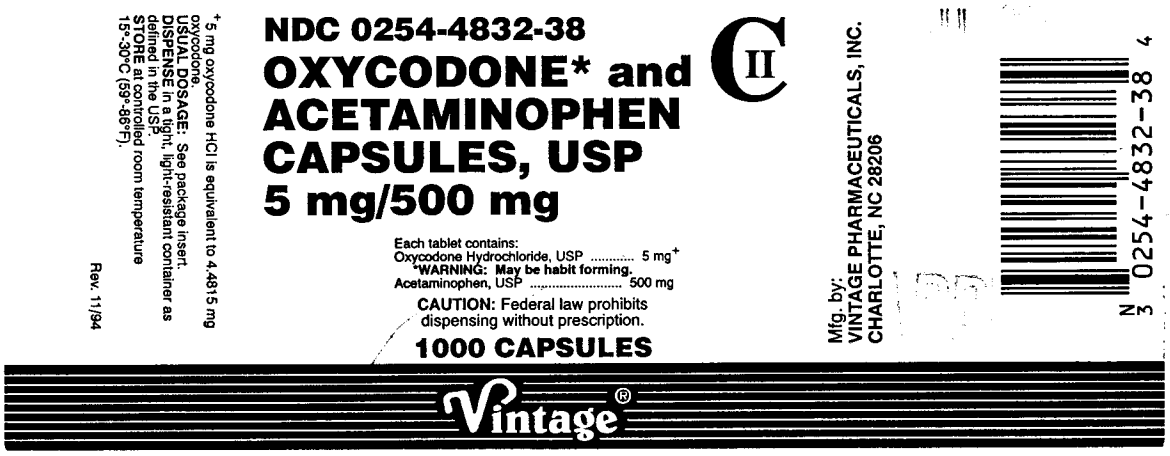
IN-69
Revised 11/95
R1

mango

VINTAGE PHARMACEUTICALS,INC
Oxycodone and Acetaminophen Capsules, USP
5 mg (as Oxycodone Hydrochloride)/500 mg
Major Amendment







CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040106

CHEMISTRY REVIEW(S)

1. CHEMIST'S REVIEW NO. 3

2. ANDA # 40-106

3. NAME AND ADDRESS OF APPLICANT

Vintage Pharmaceuticals, Inc.
3241 Woodpark Boulevard
Charlotte, NC 28206

4. LEGAL BASIS FOR ANDA SUBMISSION

Reference drug product:
Tylox (Acetaminophen/Oxycodone, 500 mg/5 mg - McNeil Pharmaceuticals, Inc.
No patents, AA product

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME

Oxycodone and Acetaminophen Tablets USP, 5 mg/500 mg

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

6-15-94: Original submission
8-10-94: Amendment
4-17-95: Amendment
4-19-95: NC
12-11-95: Amendment
6-10-96: Amendment
6-20-96: Amendment
7-09-96: Amendment (withdrawal of [redacted] /S/ [redacted] as a source of Oxycodone HCL)
7-16-96: Amendment

FDA:

6-23-94: Acknowledgement
10-28-94: 1st NA letter
11-20-95: 2nd NA letter
6-7-96: Phone NA conversation
6-26-96: Phone conversation to request to withdraw [redacted] (b)4 - [redacted] as a source of Oxycodone HCL
7-16-96: Phone NA conversation regarding total impurities NMT 2.0% in the COA for the finished product

10. PHARMACOLOGICAL CATEGORY

Analgesic for the relief of moderate to moderately severe pain.

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

(b)4 - Confidential Business

13. DOSAGE FORM

Capsules

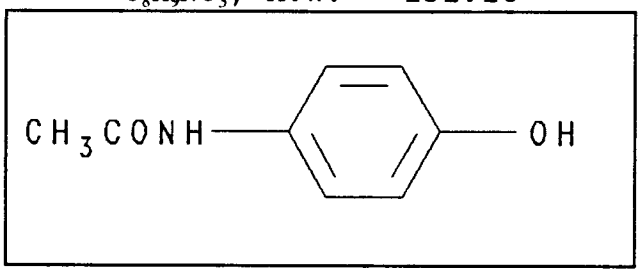
14. POTENCY

5 mg/500 mg

15. CHEMICAL NAME AND STRUCTURE

Acetaminophen USP

$C_8H_9NO_3$; M.W. = 151.16



4'-Hydroxyacetanilide. CAS [103-90-2]

Oxycodone Hydrochloride USP (see pages 1129 per USP 23 for chemical structure)

$C_{18}H_{21}NO_4 \cdot HCl$ 351.83

Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-,hydrochloride, (5α)-,

4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride [124-90-3].

16. RECORDS AND REPORTS: N/A

17. COMMENTS

Comments:

Q: 1. Regarding the components and composition:

Q: a. It is noted that "5 mg oxycodone is equivalent to 5 mg oxycodone HCl" in your unit composition statement. Please submit a correct and annotated unit composition statement.

A: OK (see Attachment I of 12-11-95 amendment).

Q: b. The components and composition statement for Oxycodone and Acetaminophen Capsules USP should be identified as Oxycodone and Acetaminophen Capsules USP, 5 mg (as Oxycodone Hydrochloride)/500 mg rather than Oxycodone and Acetaminophen Capsules USP, 5 mg/500 mg.

A: OK (see Attachment I of 12-11-95 amendment).

Q: c. Please completely describe the gelatin capsules (size and colors including body and cap) in the unit composition.

A: OK (see Attachment I of 12-11-95 amendment).

Q: d. Provide a complete list of components for imprinting ink including [redacted], Black Ink and [redacted](b)4 - [redacted], Black Ink in the composition statement and include the composition statement in the stability data report.

A: OK (see Attachment I of 12-11-95 amendment).

e. We note that synthetic black iron oxide is present in the formulation. Please provide the amount of iron oxide per capsule. This is required in order to comply with 21 CFR 1200 which limits the amount of elemental iron to not more than 5 mg per day.

A: OK (see Attachment I of 12-11-95 amendment).

Q: 2. The revised certificate of analysis for Oxycodone Hydrochloride USP from [redacted](b)4 - [redacted]ubmitted as Attachment

15 in the April 17 1995 amendment was incomplete. Please determine and include in the COA limits and test results for related substances testing (individual and total impurities) which meet USP 23 requirements.

A: OK (see Attachment II of 12-11-95 amendment).

Q: 3. We note that you wish to retain the service of [redacted] (b)4 - [redacted] for the purpose of conducting microbial testing as needed. Please provide the complete address of [redacted] and a CGMP compliance statement.

A: OK (see Attachment III of 12-11-95 amendment).

Q: 4. Please delete the revised reprocessing statements in Attachment 2 of the April 17, 1995. Be advised that approval of reprocessing requires submission of specifications and supporting data .

A: OK (see response 4 of 12-11-95 amendment and Vintage withdraws the reprocessing statement found in Attachments 2 of the April 17, 1005 amendment).

Q: 5 We note that there are no packaging batch records for the 500's package size on Lots 85113 and 86113. We require that the ANDA test batches be packaged entirely. Refer to our industry letter dated November 8, 1991 and OGD Policy and Procedure Guide #41-95 dated February 8, 1995. Please provide justification for the partial packaging and a protocol to support the partial packaging of the test batches.

A: OK (see response 5 of 12-11-95 amendment.).

6. Your application fails to present complete descriptions of the container/closure systems. In that regard:

Q: a. Submit a statement (in tabular form) containing the following information:

1) The manufacturer of the bottles for each package size (e.g., 100's and 1000's).
2) Names of all resins and materials to be used to manufacture the bottles and closures. Which resin will be used for manufacturing each size bottle?
3) Identify the manufacturer, supplier and composition for each component of your container/closure system.
4) Manufacturer of material used for inner seal.
5) Manufacturer of rayon or cotton, if

applicable.
6) Which cap is used with which bottle.
7) Which bottle is used for each package size.
8) Which pigment(s) are used in the resin for each size bottle and closure.
9) Describe any desiccant used.

This information may be referenced by authorization letters to DMF's, but you must provide a summary statement.

A: OK (see response 6a and Attachment IV of 12-11-95 amendment.).

Q: b. Submit the certification from USI chemicals that the [redacted] meets the current USP 23 Physicochemical requirements for plastic containers.

A: OK (see response 6b and Attachment V of 12-11-95 amendment.).

Q: c. Submit the certification from [redacted] that demonstrates the [redacted] meets the current USP 23 Physicochemical requirements for plastic containers.

A: OK (see response 6c and Attachment VI of 12-11-95 amendment.).

Q d. The 1500 cc container uses the [redacted] according to your cover letter of April 17, 1995. However, the 1500 cc container uses [redacted] in Attachment 33 of the 4-17-95 amendment. Please clarify.

A: OK (see response 6d and Attachment IV of 12-11-95 amendment.).

Q: 7. We note [redacted] were listed as Oxycodone HCl impurities in your COA. However these do not correlate with those listed as Oxycodone HCl impurities in DMF [redacted] Please clarify and correct.

A: OK (see response 7 and Attachments VII & VIII of 12-11-95 amendment.).

Q: 8. Your application fails to contain a satisfactory stability protocol and supporting stability data. In this regard:

Q: a The batch composition in Attachment 44 of the

April 17, 1995 is incomplete. Please include the complete formula in the stability data report (see deficiencies A.1.a. - A.1.d.).

A: OK (see response 8a and Attachment X of 12-11-95 amendment.).

Q: b. Please submit a complete and revised stability protocol specific for this drug product. Include all elements, e.g., accelerated stability, stability commitment, post-approval stability protocol (sample, schedule, testing and report format). The protocol must include a written proposal for expiration dating, identification of the stability-indicating assay method to be used, a testing schedule which specifies the tests to be performed at each test station, and the stability commitments. Please revise and resubmit.

A: OK (see response 8b and Attachments IX, X, XI, & XII of 12-11-95 amendment.).

Q: c. We note that the specifications [redacted](b)4 - [redacted] of assay for Oxycodone HCL is used in the COA for the finished drug product. However, the specifications [redacted] of assay for OXY (Oxycodone) is listed in the stability data report. Please submit data consistent with compendial requirements.

A: OK (see response 8c and Attachment X of 12-11-95 amendment.).

Q: d. Please provide the specifications of the moisture and brittleness testing rather than "report results" for the stability studies.

A: OK (see response 8d and Attachments X & IX of 12-11-95 amendment.).

Status:

a. **EER:** Pending

Requested for applicant , [redacted](b)4 [redacted] Lucia C. Tang on 10-13-94 and acceptable on 12-16-95. Updated and pre-approval EER was requested on 7-12-96 by Tim Ames with withdrawal of [redacted]

b. MV (method validation):

Methods validation is not required since active ingredients and drug product are monographs in USP.

c. Bio-Review: Satisfactory

Bio-waiver OK. Reviewer, J. Chaney on 7-28-94.

d. Labeling review: Satisfactory

Satisfactory per C Hopper and A Vezza reviewed on 6-5-96.

e. DMFs: Satisfactory

DMFs (b)4 has been reviewed and found acceptable by A. Langowski on 3/20/96. 6930 has been reviewed and found acceptable by L. Tang on 4/3/96. DMF (b)4 was reviewed and found acceptable by L. Tang on 4/3/96. However, DMF# (b)4 was withdrawn from the application on 7-8-96.

18. CONCLUSIONS AND RECOMMENDATIONS

Approval

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 7-16-96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040106

BIOEQUIVALENCE REVIEW(S)

JUL 28 1994

Oxycodone Hydrochloride/
Acetaminophen, USP
5 mg/500 mg Capsules
ANDA #40-106
Reviewer: James E. Chaney
WP# 40106DW.694

Vintage Pharmaceuticals, Inc.
Charlotte, NC
Submission Date:
June 15, 1994

Review of Dissolution Data and a Waiver Request

The firm has submitted comparative in vitro dissolution data for its drug product, Oxycodone and Acetaminophen Capsules USP, 5 mg/ 500 mg, comparing it to the reference, McNeil's Tylox® Capsules, 5 mg/500 mg, in support of a request for a waiver of in vivo bioequivalence requirements.

Comments:

1. The test drug product contains active ingredients in the same strength and dosage form as the currently approved reference product, McNeil's Tylox® Capsules, 5 mg/500 mg.

2. The dissolution method used was correct and satisfactory content uniformity data was submitted for the lot used in the dissolution testing.

3. The dissolution testing data demonstrate that the test and reference products meet the dissolution specifications (Table 1). The specifications are that not less than [redacted] of the labeled amount of oxycodone hydrochloride and not less than [redacted] of the labelled amount of acetaminophen is dissolved in 45 minutes. For both the test and reference products greater than [redacted] of the acetaminophen and greater than [redacted] of the oxycodone hydrochloride are dissolved within **15** minutes.

4. The reference product, McNeil's Tylox® Capsule, (acetaminophen/oxycodone, 500 mg/5 mg) is classified AA in "Approved Drug Products with Therapeutic Equivalence Evaluations". Therefore, since the dissolution testing is acceptable there would be no need to conduct an in vivo bioequivalence study.

5. The formulation of the test product is given in Table 2.

6. The firm did not include %CV's in its dissolution report. The %CV's were calculated by the reviewer. In any future submissions of dissolution data the firm should report these values.

Recommendations:

1. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 mL of 0.1N HCL at 37°C using USP XXII apparatus II (paddle) at 50 rpm. The test product should meet the following specifications:

   Not less than [redacted] of the labeled amount of acetaminophen and oxycodone hydrochloride in the dosage form is dissolved in 45 minutes.

2. The dissolution testing conducted by Vintage Pharmaceuticals, Inc. on its drug product, oxycodone hydrochloride and acetaminophen capsules USP, 5 mg/500 mg (lot # 85113) has been found acceptable.

3. The Division of Bioequivalence agrees that the information submitted by Vintage Pharmaceuticals, Inc. on its drug product, oxycodone hydrochloride and acetaminophen capsules USP, 5 mg/500 mg falls under 21 CFR 320.22 of the Bioavailability/Bioequivalence Regulations. The waiver of in vivo bioequivalence study for the drug is granted. From the bioequivalence point of view, the Division of Bioequivalence deems oxycodone hydrochloride and acetaminophen capsules USP, 5 mg/500 mg manufactured by Vintage Pharmaceuticals, Inc. to be bioequivalent to the reference product, Tylox® Capsules, 5 mg/500 mg manufactured by McNeil Laboratories.

The firm should be informed of the recommendations and comment 6.

[redacted] /S/

James E. Chaney, Ph. D.
Division of Bioeqivalence
Review Branch I

RD INITIALED ATWU
FT INITIALED ATWU [redacted] /S/ Date 7/28/94

cc: Anda 40-106 original, HFD-630, HFD-600 (OGD), HFD-604 (Hare), HFC-130 (Allen), HFD-652 (Wu, Chaney), Drug File

JEC/072894/ntp/WP#40106DW.694

Table 1. In Vitro Dissolution Testing

Drug (Generic Name): Oxycodone Hydrochloride/Acetaminophen
Dose Strength: 5 mg/500 mg
ANDA No.: ANDA # 40-106
Firm: Vintage Pharmaceuticals, Inc.
Submission Date: June 15, 1994
File Name: 40106DW.694

I. Conditions for Dissolution Testing:

USP XXII Basket: Paddle: X RPM: 50
No. Units Tested: 12
Medium: 0.1N HCl Volume: 900 ml
Specifications: NLT (b)4 of the oxycodone Hydrochloride in 45 min,
NLT (b)4 of the acetaminophen in 45 min.
Reference Drug: Tylox Capsules, McNeil Pharmaceuticals, Inc.
Assay Methodology: [redacted]

II. Results of In Vitro Dissolution Testing:

Oxycodone HCl

Sampling Times (Minutes)	Test Product Lot # 85113 Strength(mg) 5			Reference Product Lot # LS5347P Strength(mg) 5		
	Mean %	Range	%CV	Mean %	Range	%CV
5	83.2	(b)4 - Confidential Business	11	21.1	(b)4 - Confidential Business	55
15	96.9		3.7	85.1		12
30	97.3		2.4	103.0		4.9
45	99.7		3.1	105.2		5.7

Acetaminophen

Sampling Times (Minutes)	Test Product Lot # 85113 Strength(mg) 500			Reference Product Lot # LS5347P Strength(mg) 500		
	Mean %	Range	%CV	Mean %	Range	%CV
5	72.0	(b)4 - Confidential Business	9.4	22.6	(b)4 - Confidenti Business	38
15	89.4		4.8	76.9		8.5
30	94.8		2.4	95.4		4.8
45	98.5		1.2	97.8		6.6

Table 2.

Formulation of Vintage Pharmaceuticals' Proposed Oxycodone Hydrochloride/Acetaminophen, 5 mg/500 mg Tablets

Component	mg/Tablet
Acetaminophen 100%, USP, Dense Powder	500.00
Oxycodone HCl, USP	5.00
Croscarmellose Sodium, NF	(b)4 -
Microcrystalline Cellulose, NF	
Sodium Starch Glycolate, NF	nfiden
Magnesium Stearate, NF	
Total Weight	550.00